REMARKS

Claims 1-21 are pending in the instant application. Claims 1, 2, 16 and 17 were elected in response to the Restriction Requirement.

Rejoinder of Claims

Applicants continue to request the rejoinder of claims 8, 9, 18, and 19 directed to methods of making and using the claimed polypeptides upon allowance of a product claim per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103 (b)" which sets forth the rules, upon allowance of product claims, for the rejoinder of process claims covering the same scope of products. Therefore, Applicants respectfully maintain their request for rejoinder and examination of method claims 8, 9, 18, and 19 upon a finding of allowable subject matter in any of the product claims. The Examiner notes that rejoinder of method claims, as requested by Applicants, is being held in abeyance until such time as a finding of allowable subject matter.

Amendments to the Claims

In the interest of expediting prosecution and not for reasons related to patentability, claim 1 c) has been deleted. The amendment removes recitation of "a biologically-active fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, said polypeptide retaining at least one function of a polypeptide comprising an amino acid sequence of SEQ ID NO:1." Therefore, entry of this amendment is deemed proper and is respectfully requested in order to place the application in condition for allowance or place the application in better form for appeal.

Rejection under 35 U.S.C.§101, first paragraph and 35 U.S.C.§ 112, first paragraph

The rejection of claims 1, 2 16 and 17 is improper, as the inventions of those claims have a patentable utility as set forth in the instant specification, and/or a utility well-known to one of ordinary skill in the art. Moreover, to the extent that the rejection under § 112, first paragraph, is based on the improper allegation of lack of patentable utility under § 101, it fails for the

same reasons.

Applicants traverse these rejections for at least the reasons submitted below.

I. The Applicable Legal Standard

To meet the utility requirement of sections 101 and 112 of the Patent Act, the patent applicant need only show that the claimed invention is "practically useful," *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973) and confers a "specific benefit" on the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689 (1966). As discussed in a recent Court of Appeals for the Federal Circuit case, this threshold is not high:

> An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end").

Juicy Whip Inc. v. Orange Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999).

While an asserted utility must be described with specificity, the patent applicant need not demonstrate utility to a certainty. In *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 USPQ2d 1094 (Fed. Cir. 1991), the United States Court of Appeals for the Federal Circuit explained:

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

The specificity requirement is not, therefore, an onerous one. If the asserted utility is described so that a person of ordinary skill in the art would understand how to use the claimed invention, it is sufficiently specific. *See Standard Oil Co. v. Montedison, S.p.a.*, 212 U.S.P.Q. 327, 343 (3d Cir. 1981). The specificity requirement is met unless the asserted utility amounts to a "nebulous expression" such as "biological activity" or "biological properties" that does not convey meaningful information

about the utility of what is being claimed. *Cross* v. *Iizuka*, 753 F.2d 1040, 1048 (Fed. Cir. 1985).

In addition to conferring a specific benefit on the public, the benefit must also be "substantial." *Brenner*, 383 U.S. at 534. A "substantial" utility is a practical, "real-world" utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980).

If persons of ordinary skill in the art would understand that there is a "well-established" utility for the claimed invention, the threshold is met automatically and the applicant need not make any showing to demonstrate utility. Manual of Patent Examination Procedure at § 706.03(a). Only if there is no "well-established" utility for the claimed invention must the applicant demonstrate the practical benefits of the invention. *Id.*

Once the patent applicant identifies a specific utility, the claimed invention is presumed to possess it. *In re Cortright*, 165 F.3d 1353, 1357, 49 USPQ2d 1464 (Fed. Cir. 1999); *In re Brana*, 51 F.3d 1560, 1566; 34 USPQ2d 1436 (Fed. Cir. 1995). In that case, the Patent Office bears the burden of demonstrating that a person of ordinary skill in the art would reasonably doubt that the asserted utility could be achieved by the claimed invention. *Id.* To do so, the Patent Office must provide evidence or sound scientific reasoning. *See In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). If and only if the Patent Office makes such a showing, the burden shifts to the applicant to provide rebuttal evidence that would convince the person of ordinary skill that there is sufficient proof of utility. *Brana*, 51 F.3d at 1566. The applicant need only prove a "substantial likelihood" of utility; certainty is not required. *Brenner*, 383 U.S. at 532.

A. Identification of Biological Function or Role of an Expressed Polypeptide is Not Required to Demonstrate Utility

The Examiner agrees with Applicants' position that there is no requirement that "biological function" of the claimed polynucleotides be known to establish utility. However, the Office suggested that "*appellants* statements that there has been a requirement made that *appellants* disclose the biological function of the claimed nucleic acid is incorrect" (Office Action of May 15, 2003, page 3) (emphasis added) is also incorrect. The instant response is to a Final Office Action. A Notice of Appeal has only been submitted in conjunction with this response. Therefore the Examiner's assertion

that the instant application is under Appeal is incorrect. Applicants' respectfully request the Office's acknowledgment and correction of this statement in writing for the record.

B. The Furness Declaration Supports the "Well-Established" Utilities of NHT, and thus, at Least One Utility for SEQ ID NO:1

As a preliminary mater, Applicants note that the Examiner has not stated, for the record that the Declaration of Furness has been entered into the record. Applicants respectfully request such a statement in writing, for the record to be complete regarding the Furness Declaration.

The Examiner has asserted that the Specification does not disclose the use of NHT in gene and protein expression monitoring applications, methods well-known at the time of the filing of the parent application, March 6, 1997. However, a patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 9029 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986); MPEP § 2164.01.

In the present case, gene and protein expression monitoring applications are known by the skilled artisan to be useful in connection with drug development and monitoring the activity of drugs. Further, the skilled artisan recognizes the use of 2-D PAGE mapping in the study of protein expression and its regulation in response to drugs and toxic agents.

The Declaration of Lars Michael Furness under 37 C.F.R. § 1.132 (the Furness Declaration) was submitted in order to provide objective evidence of at least one well-established utility for the claimed invention. The Furness Declaration described some of the practical uses of the claimed polypeptides in gene and protein expression monitoring applications as they would have been understood by one of skill in the art before March 6, 1997. Further, L. Michael Furness is a recognized expert in the art, and has no interest in the outcome of this application, contrary to the allegations of the Examiner.

Thus, the Furness Declaration provides objective evidence that a person of ordinary skill in the art can achieve beneficial results from the SEQ ID NO:1 (NHT) polypeptide in the absence of any knowledge as to the precise function of the protein. The uses of the claimed polypeptides for protein

expression monitoring applications including toxicology testing are in fact independent of the function of the polypeptide. Moreover, the claimed invention has numerous other uses as a research tool, each of which alone is a "substantial utility." These include: screening libraries of pharmaceutical agents to identify those which specifically bind NHT in a variety of drug screening techniques; generating antibodies which specifically bind and can identify NHT; and titration of NHT to initially determine the effective dose in cell culture assays or in animal models. (Specification, pages 23-25, 30-31, 36 and 44). Therefore, the uses of the claimed invention in 2-D PAGE gels to assess expression of SEQ ID NO:1 in response to drugs and toxic agents and as a research tool are well known "real-world" utilities which are credible, specific and substantial utilities attributable to the claimed invention.

II. Applicants' Evidence Demonstrates to One of Ordinary Skill in the Art that NHT is More Likely Then Not a Member of the TUBBY Protein Family

Applicants' have established, and one of skill in the art would find Applicants' evidence to demonstrate that, more likely than not, NHT is a member of the TUBBY protein family. The Specification teaches that NHT shares chemical and structural sequence similarity with two TUBBY polypeptides, one from mouse (SEQ ID NO:3) and one from human (SEQ ID NO:4). In particular, NHT shares more than 49% sequence identity with both sequences over its entire length, and is nearly 70% identical with both SEQ ID NO:3 and SEQ ID NO:4, from about amino acid D187 to D436 (numbering on SEQ ID NO:1, about 249 consecutive amino acid residues) (see Specification, page 11, and Figures 2A and 2B).

The Examiner has misconstrued Applicants' and Declarant's reference to NHT as a "novel tubby homolog," citing the "art-accepted meaning of 'homologues.' See the Office Action of May 15, 2003, pages 5-6. Although the Examiner's definition of homolog is "art recognized," so too is Applicants' usage. The term homolog, as used in the instant application only, is a comparison of sequences of amino acids or proteins of distantly related species. Thus, the instant application refers to NHT as being a sequence ***homolog*** to the mouse tub gene (GI 1279766, SEQ ID NO:3) as well as sharing sequence ***similarity*** to the human tub homolog of the mouse tub gene (GI 1305497, SEQ ID NO:4) (see Specification, page 2, lines 20-22).

Specifically, SEQ ID NO:1 (NHT) is yet another human homolog of the murine tub gene, GI 1279766 (SEQ ID NO:3). However, SEQ ID NO:1 should not be construed to be a homolog of SEQ ID NO:4. Rather, SEQ ID NO:1 and SEQ ID NO:4 share sequence similarity. Additionally, SEQ ID NO:1 shares chemical and structural similarity with the human tub homolog (SEQ ID NO:4) of the murine tub gene (SEQ ID NO:3). Therefore, SEQ ID NO:1 shares chemical and structural homology with SEQ ID NO:3, the mouse tub gene, and is yet another homolog of the mouse tub gene.

A. The similarity of the claimed polypeptide to another of undisputed utility demonstrates utility beyond the reasonable probability required by law

Because the claimed NHT shares homology with the TUBBY gene family, a family in which the members have undisputed utility, evidence of homology can be used to show a substantial likelihood that the claimed polypeptide is similarly useful. Applicants need not show any more to demonstrate utility. Under the applicable law, once the applicant demonstrates a *prima facie* case of homology, the Examiner must accept the assertion of utility to be true unless the Examiner comes forward with evidence showing a person of ordinary skill would doubt the asserted utility could be achieved by a reasonable probability. *See In re Brana*, 51 F.3d at 1566-67; *In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974).

As indicated by the final Utility Examination Guidelines (66 FR 1092, January 5, 2001), where the asserted specific, substantial and credible utility for the claimed polypeptide/protein can be based upon homology to existing proteins having an accepted utility, "the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion." Applicants submit that this Office Action failed to provide sufficient evidence or sound reasoning to rebut Applicants' asserted use of the polypeptide.

In order to demonstrate utility by membership in a class, the law requires only that the class not contain a substantial number of useless members. So long as the class does not contain a substantial number of useless members, there is sufficient likelihood that the claimed invention will have utility and a rejection under 35 U.S.C. § 101 is improper. That is true regardless of how the claimed invention ultimately is used and whether the members of the class possess one utility or many. *See Brenner* v.

Manson, 383 U.S. 519, 532 (1966); *Application of Kirk*, 376 F.2d 936, 943 (CCPA 1967); *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973).

In fact, at a recent Biotechnology Customer Partnership Meeting held at the USPTO on April17, 2001, in a talk by Senior Examiner James Martinell, it was emphasized that Applicants' assertion that his claimed protein "is a member of a family of proteins that [is] already known based upon amino acid sequence homology" can be effective as an assertion of utility for the claimed sequence. According to Dr. Martinell, the proper question for the Examiner to ask, after searching the prior art for the claimed protein, is "Would one of skill in the art accept that the protein has been placed in the correct family of proteins as is asserted?" The "two" [sic: three] possible answers that can be deduced from this prior art search are, according to Dr. Martinell:

- The search does not reveal any **evidence** that the family attribution made in the application is either **incorrect or may be incorrect**
- The protein either **more likely belongs to a family other than that asserted** in the application or **likely does not belong to the family asserted** in the application
- The search shows that the attribution is likely correct

(From handouts of Dr. Martinell's slides distributed April 17, 2001; emphasis added)

This Office Action has failed to meet the above requirements now recognized by the USPTO. No evidence is cited particular to the claimed protein, e.g., inconsistent findings deduced from the search, upon which to base any objection to the assignment of functional homology to this family of TUBBY proteins. Indeed, there is no such evidence.

In this regard, NHT is ***similar*** to two TUBBY polypeptides, one from mouse (SEQ ID NO:3) and one from human (SEQ ID NO:4). In particular, NHT shares more than 49% sequence identity over 491 amino acid residues, and is in fact nearly 70% identical with the two sequences from about amino acid D187 to D436 (about 249 amino acid residues) (see specification, page 11, and Figures2 A and 2B).

This is more than enough homology to demonstrate a reasonable probability that the utility of the human TUBBY polypeptides can be imputed to the claimed invention. It is well-known that the probability that two unrelated polypeptides share more than 40% sequence homology over 70 amino acid residues is exceedingly small. Brenner et. al., Proc. Natl. Acad. Sci. 95:6073-78 (1998)

(Reference No. 5, of record). Given homology in excess of 40% over many more than 70 amino acid residues, the probability that the claimed polypeptide is related to the human TUBBY polypeptides is, accordingly, very high. Additional studies by others of the *TUB* gene family provide further evidence that NHT is a member of the TUBBY protein family.

Applicants submitted in their response of December 13, 2002, the results of a recent BLASTP analysis of SEQ ID NO:1 verses the genpept database (NCBI, version 132). Those results were apparently disregarded by the Office. Had the Office examined the analysis, it would have been obvious that SEQ ID NO:1 has **99%** identity, from residue M1 to residue I439 to tubby-like protein 3 (TULP3, GI21618457), and from 49% to 93% sequence identity to nine additional proteins, all of which are either tubby proteins, TUB homologs, or tubby homologs from either human or mouse (Exhibit A). Clearly, one of ordinary skill in the art would find such evidence to corroborate Applicants' assertion that SEQ ID NO:1 is a member of the TUBBY protein family.

The tubby-like protein 3 has recently been shown to function in signal transduction from heterotrimeric G protein-coupled receptors (Santagata, S. *et al.* (2001) Science 292:2041-2050, Exhibit B, of record). Such a function would more likely than not be applicable to SEQ ID NO:1 as well. Clearly, this is credible, scientific evidence that one skilled in the art would more likely than not conclude that SEQ ID NO:1 is a member of the TUBBY protein family that functions in signal transduction from heterotrimeric G protein-coupled receptors, as seen by the high conservation of residues at the C-terminus.

The Office's citation of Wistow et al. is moot, as Applicants' have never asserted that SEQ ID NO:1 and SEQ ID NO:4 have the same biological function (Office Action of May 15, 2003, page 6). Moreover, the teachings of Wistow et al. have no relevance to the instant application. Wistow et al. address heat-shock proteins and lens crystallins, in contrast, the instant application is directed to a novel TUBBY homolog (Specification, page 2, lines 20-22). SEQ ID NO:1 is yet another homolog of the murine Tubby protein (SEQ ID NO:3) and shares sequence identity with human Tub (SEQ ID NO:4).

Thus, Applicants' have provided corroborating evidence which one of skill in the art would find more likely than not that SEQ ID NO:1 is yet another homolog to the mouse TUBBY polypeptide and a member of the TUBBY protein family. Therefore, Applicants have met the standard of proof and the

Office's evidence to the contrary refuting Applicants' findings is not applicable.

It is undisputed that the claimed polypeptide is a protein having the sequence shown as SEQ ID NO:1 in the patent application and referred to as NHT in the application. Moreover, since there is a substantial likelihood that the claimed polypeptide is a member of the TUBBY gene family, and the members are indisputably useful, there is by implication a substantial likelihood that the claimed polypeptide is similarly useful. Applicants need not show any more to demonstrate utility. Therefore, the Examiner must accept applicants' demonstration that the claimed polypeptide is a member of the TUBBY proteins and that the utility is proven by a reasonable probability unless the Examiner can demonstrate through evidence or sound scientific reasoning that a person of ordinary skill in the art would doubt utility. *See In re Langer*, 503 F.2d 1380, 1391-1392, 183 USPQ 288 (CCPA 1974).

The final Utility Examination Guidelines further provides that

> [w]hen a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein.

This Office Action offers no evidence that the members of this class of TUBBY proteins do not share a specific, substantial functional attribute or utility, despite having structural features in common. Thus, this strongly indicates that any member of this TUBBY protein class would have some patentable utility. It follows that there is a more substantial likelihood that the claimed polypeptide also has a patentable utility, regardless of its actual function. The law has never required a patentee to prove more.

It appears from the statements of the Office Action that Applicants are being required to assert a rigorous correlation to establish the identity of NHT as a member of the TUBBY family as well as to establish a specific disease affected by NHT. However, the final Utility Examination Guidelines provides that

> [A] "rigorous correlation" need not be shown in order to establish practical utility; "reasonable correlation" is sufficient. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed Cir. 1996).

The Examiner must accept the applicants' demonstration that the homology between the claimed invention and TUBBY polypeptides demonstrates utility by a reasonable probability, and additionally, that the claimed polypeptide is a member of the TUBBY gene family unless the Examiner can demonstrate through evidence or sound scientific reasoning that a person of ordinary skill in the art would doubt utility. *See In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974). The Examiner has not provided sufficient evidence or sound scientific reasoning to the contrary.

1. SEQ ID NO:1 has the Utility of TULP3

The Office has refused to accept that 99% sequence identity between SEQ ID NO:1 and TULP3 provides a utility for SEQ ID NO:1, i.e., functioning in signal transduction from heterotrimeic G protein coupled receptors (Office Action of May 15, 2003, page 8). The Examiner offers no basis to support the Examiner's disbelief of Applicants' asserted function. Given this lack of explicit support, Applicants can only assume that the Examiner is relying on facts within her personal knowledge that lead her to disregard the proffered evidence. She is in effect holding herself out as one of ordinary skill in the art. Thus, Applicants request an affidavit from the Examiner in support of this basis for rejection, in keeping with 37 C.F.R. §104(d)(2).

2. Constructive Reduction to Practice Constitutes Conception of Utility

Applicants' constructive reduction to practice of the instant application constitutes good and sufficient conception of the utility of SEQ ID NO:1 as disclosed in the instant application. However, the Office asserts that the Santagata et al., 2001 paper is a "post-filing date, and cannot be relied upon to establish what was known about TULP proteins at the time the invention was made" (Office Action of May 15, 2003, page 9).

The instant application is replete with disclosures of functions for SEQ ID NO:1. Applicants' assertion that TUBBY proteins are involved in appetite and eating disorders is based on the function of the murine Tubby homolog (SEQ ID NO:3). So too, SEQ ID NO:1, again based on its homology to murine tubby (SEQ ID NO:3), finds additional uses by virtue of the association of Tubby with progressive retinal degeneration and hearing loss, as well as maturity onset diabetes and insulin resistance. Further, sensory defects may be associated with cGMP induced, phosphodiesterase mediated apoptotic activity (See Specification, page 2, lines 9-13). Thus, SEQ ID NO:1 also finds use

in the study of ocular diseases.

B. The Office has Failed to Consider All Evidence Presented by Applicants to Establish Utility for the Claimed Invention

The Examiner has asserted that Applicants cannot rely upon the Santagata et al. 2001 publication, because it is a "post-filing date, and cannot be relied upon to establish what was known about TULP proteins at the time the invention was made" (Office Action of May 15, 2003, page 9). It is Applicants' position that the Santagata et al. paper is further ***supporting evidence*** that SEQ ID NO:1 is a member of the Tubby gene family. Such evidence is required to be given "due consideration."

Section 2701.02 of Manual of Patent Examining Procedure (original 8th edition, published August, 2001, latest revision February 2003) (hereinafter "MPEP") provides:

> If a rejection under 35 U.S.C. 101 has been properly imposed, along with a corresponding rejection under 35 U.S.C. 112, first paragraph, the burden shifts to the applicant to rebut the prima facie showing. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992) ("The examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a prima facie case of unpatentability. . . . After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, ***by a preponderance of evidence with due consideration to persuasiveness of argument***."). ***An applicant can do this using any combination of the following: amendments to the claims, arguments or reasoning, or new evidence submitted in an affidavit or declaration under 37 CFR 1.132, or in a printed publication***. . . . (emphasis added)
>
> If the applicant responds to the prima facie rejection, Office personnel should review the original disclosure, any evidence relied upon in establishing the prima facie showing, any claim amendments, and any new reasoning or evidence provided by the applicant in support of an asserted specific and substantial credible utility. It is essential for Office personnel to recognize, fully consider and respond to each substantive element of any response to a rejection based on lack of utility. Only where the totality of the record continues to show that the asserted utility is not specific, substantial, and credible should a rejection based on lack of utility be maintained. ***If the record as a whole would make it more likely than not that the asserted utility for the claimed invention would be considered credible by a person of ordinary skill in***

> ***the art, the Office cannot maintain the rejection. In re Rinehart, 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976).*** (emphasis added)

Id at page 2100-42-43.

Applicants' reiterate in their entirety arguments and reasoning presented to the Office in their response filed December 13, 2002 pertaining not only to the membership of SEQ ID NO:1 in the tubby gene family, but also evidence of the function of TULP3 and therefore, more likely than not, an asserted function and utility for SEQ ID NO:1. Applicants respectfully ask the Office to abide by the practices set forth in the MPEP and established by case law.

C. Membership in a Class of Useful Products Can Be Proof of Utility

Despite evidence that the claimed polypeptide is a member of the TUBBY gene family, whose members indisputably are useful, the Examiner refused to impute the utility of the members of the TUBBY gene family to NHT. In the Office Action of September 24, 2002, the Patent Examiner takes the position that, "[t]he assertion that the disclosed NHT has biological activities similar to known TUBBY cannot be accepted in the absence of supporting evidence, because the relevant literature reports examples of polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities." (Office Action of September 24, 2002, page 3, ¶ 3). To demonstrate utility by membership in the class of TUBBY polypeptides, the Examiner would require that all TUBBY polypeptides possess a "common" utility.

The Examiner has not provided any evidence that any member of the TUBBY gene family, let alone a substantial number of those members, is not useful. In such circumstances the only reasonable inference is that the claimed polypeptide must be, like the other members of the TUBBY gene family, useful.

Even if the Examiner's "common utility" criterion were correct, the TUBBY gene family would meet it. It is undisputed that known members of the TUBBY gene family function in signal transduction from heterotrimeric G protein-coupled receptors. A person of ordinary skill in the art need not know any more about how the claimed invention functions in signal transduction from heterotrimeric G

protein-coupled receptors to use it, and the Examiner presents no evidence to the contrary. Instead, the Examiner makes the conclusory observation that a person of ordinary skill in the art would need to know whether, for example, any given TUBBY polypeptide functions in signal transduction from heterotrimeric G protein-coupled receptors. The Examiner then goes on to assume that the only use for NHT absent knowledge as to how this member of the TUBBY gene family actually works is further study of NHT itself. However, this assumption is incorrect.

As disclosed by Applicants, knowledge that NHT is a TUBBY-like polypeptide is more than sufficient to make it useful for the diagnosis and treatment of appetite and eating disorders and ocular diseases. Indeed, NHT has been shown to be expressed in brain, neuronal and lymph node cDNA libraries. The Examiner must accept these facts to be true unless the Examiner can provide evidence or sound scientific reasoning to the contrary. But the Examiner has not done so.

D. The Patent Examiner Failed to Demonstrate That a Person of Ordinary Skill in the Art Would Reasonably Doubt the Utility of the Claimed Invention

Applicants have shown that NHT shares homology with the TUBBY gene family, a family consisting of members known to have undisputed utility, and therefore, homology can be used to show a substantial likelihood that the claimed polypeptide is similarly useful. Applicants need not show any more to demonstrate utility. Specifically, the TUBBY family includes TULP3 which shares 99% sequence identity with NHT. TULP3 has been demonstrated to function in signal transduction from heterotrimeric G protein-coupled receptors. Based on the high level of sequence homology, structural characteristics and tissue expression, Applicants have demonstrated a *prima facie* case for homology as an acceptable assertion of utility of the claimed polypeptides. Such an assertion of utility would be determined to be sound scientific reasoning by one skilled in the art. Therefore, the Examiner must accept the applicants' demonstration by homology that the claimed polypeptide is a member of the TUBBY gene family and that the homology between the claimed invention and TUBBY polypeptides demonstrates utility by a reasonable probability, unless the Examiner can demonstrate through evidence or sound scientific reasoning that a person of ordinary skill in the art would doubt utility.

Under the applicable law, once the applicant demonstrates a *prima facie* case of homology,

the Examiner must accept the assertion of utility to be true unless the Examiner comes forward with evidence showing a person of ordinary skill would doubt the asserted utility could be achieved by a reasonable probability. *See In re Brana*, 51 F.3d at 1566; *In re Langer*, 503 F.2d 1380, 1391-92, 183 USPQ 288 (CCPA 1974).

Moreover, as indicated by the final Utility Examination Guidelines (66 FR 1092, January 5, 2001), where the asserted specific, substantial and credible utility for the claimed polypeptide/protein can be based upon homology to existing proteins having an accepted utility, "the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion." Applicants submit that this Office Action failed to provide sufficient evidence or sound reasoning to rebut Applicants' asserted use of the polypeptide.

The literature cited by the Examiner *infra* is not inconsistent with the Applicants' proof of homology by a reasonable probability. It may show that Applicants cannot prove function by homology with **certainty**, but Applicants need not meet such a rigorous standard of proof. The literature cited identifies some of the difficulties involved in predicting biological activity, or membership in a protein family, though none suggest that functional homology cannot be inferred by a reasonable probability as in this case. The Examiner rejected the pending claims on the ground that the applicant cannot "credibly" impute utility to the claimed invention based on its 49% homology to another polypeptide undisputed by the Examiner to be useful. The Examiner's rejection is both incorrect as a matter of fact and as a matter of procedural law.

In the present case, the Office Action alleges that the amino acid sequence identity between NHT and known TUBBY proteins is insufficient to establish that NHT is a member of the TUBBY family of proteins because "[t]he assertion that the disclosed NHT has biological activities similar to known TUBBY cannot be accepted in the absence of supporting evidence, because the relevant literature reports examples of polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities" (Office Action, filed September 24, 2002, page 3). The Examiner cites Tischer *et al.* (U.S.Patent 5,194,596), Benjamin *et al.* (1998), Vukicevic *et al.* (1996), North *et al.* (1997), Gu *et al.* (1998) and Hayes *et al.* (1998) as support to doubt Applicants asserted utility. Importantly, all of these documents fail to ***specifically*** support the outstanding rejections

because none of them are specifically relevant to the TUBBY protein family. Moreover, none of them contradict Brenner's basic rule that sequence homology in excess of 40% over 70 or more amino acid residues yields a high probability of functional homology as well. At most, these articles individually and together stand for the ***general*** proposition that it is difficult to make predictions about function or biological activity with certainty.

The Examiner further cited Haynes *et al.* in support of the Examiner's assertion that nucleic acid levels are not predictive of protein levels. The Northern data presented by Applicants represents evaluation of human tissue expression patterns. The Haynes *et al.* conclusion is based on the yeast *Saccharomyces cerevisiae* growing at mid-log phase, and is therefore of very limited relevance. Only 80 *S. cerevisiae* (vs. human) proteins were selected for evaluation. No where is it taught that NHT was one of the proteins evaluated. Therefore, the Haynes *et al.* paper does not teach the expression levels of SEQ ID NO:1 and does not teach away from Applicants' position that SEQ ID NO:1 was expressed in brain and neuronal tissues and in lymph node tissues. Additionally, the findings of Santagata *et al.* support Applicants' assertions that expression of SEQ ID NO:1 is predominately located in the brain.

Thus, the Haynes *et al.* paper is utterly irrelevant to the instant invention. The Examiner has attempted to broadly apply a citation which does not teach Applicants' invention. This citation does not constitute either evidence or sound scientific reasoning to show that a person of ordinary skill in the art would reasonably doubt Applicants' invention lacked patentable utility.

The Office's attention is further directed to Brenner *et al.*, *supra* that teaches through exhaustive analysis of a data set of proteins with **known** structural and functional relationships and with **<90%** overall sequence identity, that 30% identity has been determined to be a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. (Brenner *et al.*, pages 6073 and 6076.) As shown in the Figures and as discussed in the specification, SEQ ID NO:1 shares 49% identity with at least two known TUBBY proteins over at least 491 residues, and nearly 70% identity over 249 residues, vastly exceeding this threshold. Moreover, recent BLASTP analysis actually confirms that NHT is a homolog of TULP-3, by demonstrating that 99% sequence identity exists between the two proteins. Since these criteria are based on a data set of

known homologous proteins with shared structural and functional features, one of ordinary skill in the art would reasonably expect the polypeptides of the invention possess the evolutionarily conserved **structural and functional** characteristics of a TUBBY protein.

It is known in the art that natural selection acts to conserve protein function. Conversely, mutations that reduce or abolish protein function are usually eliminated by natural selection. Based on these central tenets of molecular evolution, applicants put forth that the amino acid differences among Applicants' polypeptide and the known TUBBY proteins, are likely to occur at positions of minimal functional importance, while residues that are conserved are likely those that are important for protein function. One of ordinary skill in the art would therefore conclude that, more likely than not, the level of conservation observed between Applicants' polypeptide and the two known human TUBBY proteins are indicative of a common function, and hence common utility, among these proteins.

In conclusion, the preponderance of evidence therefore does not support the Examiner's basis for the rejection of claims under 35 U.S.C. § 101. The only relevant evidence of record shows that a person of ordinary skill in the art would not doubt that the claimed polypeptide is in fact a member of the TUBBY family of proteins, which are known to have specific utility.

IV. The diagnosis and treatment of maturity onset diabetes, insulin resistance, progressive retinal degeneration and hearing loss as well as appetite and eating disorders are sufficient utilities under 35 U.S.C. §§ 101 and 112, first paragraph

The claimed invention meets all of the necessary requirements for establishing a credible utility under the Patent Law: tThere are "well-established" uses for the claimed invention known to persons of ordinary skill in the art, and there are specific practical and beneficial uses for the invention disclosed in the patent application's specification. Additionally, these uses are explained, in detail, in the Furness Declaration, discussed *supra*. Objective evidence, not considered by the Patent Office, further corroborates the credibility of the asserted utilities.

The specification teaches that NHT is a member of the TUBBY polypeptide family and that defects in *TUB* genes and in TUBBY expression have been found in maturity onset diabetes, insulin resistance, progressive retinal degeneration and hearing loss (see specification, page 2, lines 9-10).

Applicants have presented evidence that the claimed invention would have the utilities of TUBBY proteins, proteins which are known to be involved in appetite and eating disorders. Therefore, one of ordinary skill in the art would conclude that, more likely than not, that NHT would also have these uses. Thus, the claimed invention meets the utility requirements under 35 U.S.C. §§ 101 and 112, first paragraph.

V. By Requiring the Patent Applicant to Assert a Particular or Unique Utility, the Patent Examination Utility Guidelines and Training Materials Applied by the Patent Examiner Misstate the Law

There is an additional, independent reason to withdraw the rejections. To the extent the rejections are based on Revised Interim Utility Examination Guidelines (64 FR 71427, December 21, 1999), the final Utility Examination Guidelines (66 FR 1092, January 5, 2001) and/or the Revised Interim Utility Guidelines Training Materials (USPTO Website www.uspto.gov, March 1, 2000), the Guidelines and Training Materials are themselves inconsistent with the law.

The Training Materials, which direct the Examiners regarding how to apply the Utility Guidelines, address the issue of specificity with reference to two kinds of asserted utilities: "specific" utilities, which meet the statutory requirements, and "general" utilities, which do not. The Training Materials define a "specific utility" as follows:

> A [specific utility] is *specific* to the subject matter claimed. This contrasts to *general* utility that would be applicable to the broad class of invention. For example, a claim to a polynucleotide whose use is disclosed simply as "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

The Training Materials distinguish between "specific" and "general" utilities by assessing whether the asserted utility is sufficiently "particular," *i.e.*, unique (Training Materials at p.52) as compared to the "broad class of invention." (In this regard, the Training Materials appear to parallel the view set forth in Stephen G. Kunin, Written Description Guidelines and Utility Guidelines, 82 J.P.T.O.S. 77, 97 (Feb. 2000) ("With regard to the issue of specific utility the question to ask is

whether or not a utility set forth in the specification is *particular* to the claimed invention.").)

Such "unique" or "particular" utilities never have been required by the law. To meet the utility requirement, the invention need only be "practically useful," *Natta*, 480 F.2d 1 at 1397, and confer a "specific benefit" on the public. *Brenner*, 383 U.S. at 534. Thus incredible "throwaway" utilities, such as trying to "patent a transgenic mouse by saying it makes great snake food," do not meet this standard. Karen Hall, Genomic Warfare, The American Lawyer 68 (June 2000) (quoting John Doll, Chief of the Biotech Section of USPTO).

This does not preclude, however, a general utility, contrary to the statement in the Training Materials where "specific utility" is defined (page 5). Practical real-world uses are not limited to uses that are unique to an invention. The law requires that the practical utility be "definite," not particular. *Montedison,* 664 F.2d at 375. Applicant is not aware of any court that has rejected an assertion of utility on the grounds that it is not "particular" or "unique" to the specific invention. Where courts have found utility to be too "general," it has been in those cases in which the asserted utility in the patent disclosure was not a practical use that conferred a specific benefit. That is, a person of ordinary skill in the art would have been left to guess as to how to benefit at all from the invention. In *Kirk*, for example, the CCPA held the assertion that a man-made steroid had "useful biological activity" was insufficient where there was no information in the specification as to how that biological activity could be practically used. *Kirk*, 376 F.2d at 941.

The fact that an invention can have a particular use does not provide a basis for requiring a particular use. *See Brana*, *supra* (disclosure describing a claimed antitumor compound as being homologous to an antitumor compound having activity against a "particular" type of cancer was determined to satisfy the specificity requirement). "Particularity" is not and never has been the *sine qua non* of utility; it is, at most, one of many factors to be considered.

As described *supra*, broad classes of inventions can satisfy the utility requirement so long as a person of ordinary skill in the art would understand how to achieve a practical benefit from knowledge of the class. Only classes that encompass a significant portion of nonuseful members would fail to meet the utility requirement. *Supra* § III.B. (*Montedison,* 664 F.2d at 374-75).

The Training Materials fail to distinguish between broad classes that convey information of

practical utility and those that do not, lumping all of them into the latter, unpatentable category of "general" utilities. As a result, the Training Materials paint with too broad a brush. Rigorously applied, they would render unpatentable whole categories of inventions heretofore considered to be patentable, and that have indisputably benefitted the public, including the claimed invention. See *supra* § III.B. Thus, the Training Materials cannot be applied consistently with the law.

VI. To the extent the rejection of the claimed invention under 35 U.S.C. § 112, first paragraph, is based on the improper rejection for lack of utility under 35 U.S.C. § 101, it must be withdrawn.

The rejection set forth in the Office Action is based on the assertions discussed above, i.e., that the claimed invention lacks patentable utility. To the extent that the rejection under § 112, first paragraph, is based on the improper allegation of lack of patentable utility under § 101, it fails for the same reasons.

Applicants respectfully submit that rejections for lack of utility, based *inter alia*, on an allegation of "lack of specificity," as set forth in the Office Action and as justified in the Revised Interim and final Utility Guidelines and Training Materials, are not supported in the law. Neither are they scientifically correct, nor supported by any evidence or sound scientific reasoning. These rejections are alleged to be founded on facts, yet those facts are clearly distinguishable from the facts of the instant application, and indeed most if not all nucleotide and protein sequence applications. Nevertheless, the PTO is attempting to mold the facts and holdings of these prior cases, "like a nose of wax,"[1] to target rejections of claims to polypeptide and polynucleotide sequences, as well as to claims to methods of detecting said polynucleotide sequences, where biological activity information has not been proven by laboratory experimentation, and they have done so by ignoring perfectly acceptable utilities fully disclosed in the specifications as well as well-established utilities known to those of skill in the art. As is

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[1]"The concept of patentable subject matter under §101 is not 'like a nose of wax which may be turned and twisted in any direction * * *.' *White v. Dunbar*, 119 U.S. 47, 51." *(Parker v. Flook,* 198 USPQ 193 (US SupCt 1978))

disclosed in the specification, and even more clearly, as one of ordinary skill in the art would understand, the claimed invention has well-established, specific, substantial and credible utilities. The rejections are, therefore, improper and should be withdrawn.

Moreover, to the extent the above rejections were based on the Revised Interim and final Examination Guidelines and Training Materials, those portions of the Guidelines and Training Materials that form the basis for the rejections should be determined to be inconsistent with the law.

Rejection under 35 U.S.C. §112, first paragraph, written description

Claims 1 and 16 stand rejected under the first paragraph of 35 U.S.C. §112 for allegedly containing subject matter "not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons cited in the previous Office Action paper number 7, at pages(s) 6-7." The Office Action asserts that:

- . . . the specification provides SEQ ID NO: 1. No naturally occurring variants thereof are described, . . . (Office Action of September 9, 2002, page 6).

- . . . No other naturally occurring sequences have been described as obtainable from human, nor any other animal. A breadth of 90% would reasonably be expected to encompass homologues obtained from other primate species such as macaque, rhesus, gibbon, as well as from non-primate species, such as rat or mouse, giraffe, hippo or even frog or yeast, depending upon the evolutionary conservation of the protein in question (Office Action of May 15, 2003, p. 11)

- . . . There is no description of the function of the protein, such as would allow one of skill in the art to predict what portions of the disclosed sequence would be expected to be conserved. With further respect to this issue, it is a protein that is being claimed; without having a written description of all naturally occurring sequences within the metes and bounds of the claims, one would not be capable of determining whether or not a given species was claimed (Office Action of May 15, 2003, pages. 11-12)

- At page 34, appellants argue that one of ordinary skill in the art would recognize naturally occurring variants of SEQ ID NO: 1 having 90% identity to SEQ ID NO: 1; this is not true. One could certainly determine whether a

> protein that one had obtained from nature were 90% identical to SEQ ID NO: 1, but that same person, handed a protein in a test tube, would have no way of determining whether that protein were 'naturally occurring' (Office Action of May 15, 2003, page 12)

This rejection is respectfully traversed.

Applicants reiterate their arguments filed December 13, 2002. Clearly, it appears that the Examiner has apparently confused this instant application and the responses filed by Applicants with those by another. Applicants respectfully request that the Examiner fully review the response filed December 13, 2002, especially pages 33-36 as well as the Office Action Summary (Paper #7) which indicate that the Office Action of September 24, 2002 was a non-final action and thus Applicants are not Appellant(s). A written statement of this fact, for the record is respectfully requested.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. § 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

> . . . Mention of representative compounds encompassed by generic claim language ***clearly is not required by Section 112 or any other provision of the statute***. But, where no explicit description of a generic invention is to be found in the specification...mention of representative compounds may provide an implicit description upon which to base generic claim language. *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970) [emphasis added]

> . . . [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, ***it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'*** *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960) [emphasis added]

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination

of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., ***complete or partial structure***, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. ***If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.*** [emphasis added] [footnotes omitted

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

I. The specification provides an adequate written description of the claimed "variants" of SEQ ID NO:1

The subject matter encompassed by Claims 1 and 16 are either disclosed by the specification or conventional or well known to one skilled in the art.

Independent claim 1 recites "An isolated polypeptide selected from the group consisting of: a) a polypeptide comprising an amino acid sequence of SEQ ID NO:1, and b)a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said polypeptide retaining at least one function of a polypeptide comprising an amino acid sequence of SEQ ID NO:1." The Examiner's position is based upon the theory that the Specification provides an adequate written description of SEQ ID NO:1 and that "One could certainly determine whether a protein that one had obtained from nature were 90% identical to SEQ ID NO: 1(Office Action of May 15, 2003). However, the Specification allegedly lacks an adequate written description of the variant polypeptides because, "No naturally occurring variants thereof are described" (Office Action of September 24, 2002 at page 6). Applicants strongly disagree with this position.

Such a position ignores that the polypeptides recited in claim 1) ***are*** described in terms of their

structure. That is, the claimed polypeptides are "***at least 90% identical to the amino acid sequence of SEQ ID NO:***1." The structure of SEQ ID NO:1 is provided in the specification, for example, at pages 46-47 of the Sequence Listing and Figures 1A, 1B, 1C and 1D for SEQ ID NO:1. The phrases "percent identity" or "% identity" as well as methods for determining such identity are well known to the skilled artisan. Claim 1, as previously amended, does not encompass any peptide or protein with altered sequence, but rather is limited to those having at least 90% amino acid sequence identity to SEQ ID NO:1.

Applicants submit that this description is sufficient to describe the claimed genus based on the disclosure of the single species, SEQ ID NO:1, for reasons stated in the USPTO's own training materials for implementation of the Written Description Guidelines under 35 USC § 112, first paragraph. In the "Synopsis of Application of Written Description Guidelines" (USPTO Website www.uspto.gov, March 1, 2000), at page 53 of these guidelines, a claim to "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B" is considered to meet the written description requirements because:

> --- procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify all other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art.

The Guidelines further state:

> The single species disclosed (SEQ ID NO:3) is representative of the genus because all member have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity.

A detailed description of the chemical and structural features of SEQ ID NO:1 which contribute to the characterization of SEQ ID NO:1 and other related proteins related to the TUBBY gene family are provided, for example, at p. 11, lines 1-10 and Figures 2A, 2B, 3A and 3B. Ninety percent variants of the claimed polypeptides are described, for example, at p. 11, lines 13-15.

When provided with the detailed description as noted above, one of ordinary skill in the art "would have understood the inventor to be in possession of the claimed invention at the time of filing".

That is, one of ordinary skill in the art would recognize polypeptide sequences which are variants at least 90% identical to SEQ ID NO:1. Given a polypeptide sequence, it would be routine for one of skill in the art to recognize whether it was a variant of SEQ ID NO:1 and to determine the % identity to SEQ ID NO:1 of the variant. Accordingly, the specification provides an adequate written description of the recited variants of SEQ ID NO:1.

II. The specification provides an adequate written description as required by law

Applicants submit that case law in the area of the written description requirement of 35 U.S.C. 112, first paragraph is clear with regard to the details considered sufficient to describe a claimed genus:

> . . . Mention of representative compounds encompassed by generic claim language ***clearly is not required by Section 112 or any other provision of the statute***. But, where no explicit description of a generic invention is to be found in the specification . . . mention of representative compounds may provide an implicit description upon which to base generic claim language. *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970) [emphasis added]

> . . . [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, ***it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'*** *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960) [emphasis added]

The specification sets forth a description of the claimed polypeptide variants using "other appropriate language" as indicated above in connection with the remarks regarding an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1". The claimed variants have been described in terms of their relationship to the chemical structure of SEQ ID NO:1 and structural requirements at, for example, pp. 46-47 of the Sequence Listing; Figures 1A, 1B, 1C, and 1D; p. 11, lines 1-10 and Figures 2A, 2B, 3A and 3B. The specification provides a means of identifying functional variants having 90% sequence identity with SEQ ID NO:1 at, for example, p. 11, lines 1-10. Applicants therefore submit that the "genus is sufficiently identified in [the instant] application by 'other appropriate language'" as stated in *In re Grimme*, 274 F.2d 949, 952, 124

USPQ 499, 501 (CCPA 1960). Furthermore, Applicants submit that "a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing" as stated in the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001. Accordingly, Claim 2 meets the statutory requirements for written description under 35 U.S.C. 112, first paragraph.

III. Conclusion

The Final Office Action failed to base its written description inquiry pertinent to the present claims in view of their scope. In particular, the subject matter of the claims of the instant application is defined in terms of the chemical structure of SEQ ID NO:1. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polypeptides defined by the present claims is adequately described, as evidenced by specific passages of the specification as set forth above. Furthermore, the Examiner has applied to the subject application a written description standard that has no basis in the law.

For at least the above reasons it is believed that Claims 1 and 16 meet the written description requirement of 35 U.S.C. § 112, first paragraph. It is therefore requested that this rejection be withdrawn.

Rejection under 35 U.S.C. §112, second paragraph, for indefiniteness

Claims 1, 2, 16 and 17 were rejected as indefinite for allegedly "failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention" and further that, "[a]s no naturally occurring sequences having 90% identity to Seq ID NO: 1 are described, the metes and bounds of claim 1 cannot be determined. It cannot be determined which 90% identical sequences are or are not naturally occurring" (Office Action of May 15, 2003, pages 12-13). The Examiner stated that "[t]he sequence and structural properties in no way reveal the origin of the molecule or its forebears," and [c]laims 2, 16 and 17 are rejected for depending from an indefinite claim." (Office

Action of May 15, 2003, page 13).

The standard for "definiteness" is that the claims define patentable subject matter with a reasonable degree of precision and particularity. See *In re Miller*, 169 USPQ 597, 599 (CCPA 1971); *In re Moore*, 169 USPQ 236, 238 (CCPA 1971). See also MPEP §706.03(d). In this regard, the Supreme Court has indicated that the primary purpose of claim language is to give "fair" notice of what would constitute the infringement of a claim. See *United Carbon Co. v. Binny & Smith Co.*, 317 U.S. 228, 55 USPQ 381 (1942). In other words, the basic purpose of 35 U.S.C. §112, second paragraph is to require a claim to reasonably apprize those skilled in the art of the scope of the invention defined by that claim and give fair notice of what constitutes infringement of the claim. See *Antonious v. Pro Group Inc.*, 217 USPQ 875, 877 (6th Cir. 1983).

One of skill in the art, when reading the Specification, would understand the meaning of the claims. "Naturally occurring" would be understood by one of skill in the art and even by an unskilled person of the art to be that which occurs in nature. Moreover, the Specification at page 11 describes the term "fragment" as meaning:

> The term "portion", as used herein, with regard to a protein (as in "a portion of a given protein") refers to fragments of that protein. The fragments may range in size from four amino acid residues to the entire amino acid sequence minus one amino acid. Thus, a protein "comprising at least a portion of the amino acid sequence of SEQ ID NO:1" encompasses the full-length human NHT and fragments thereof. (Specification, page 8, lines 21-25)

When interpreting the claims in light of the specification, claim 1 b) claims "a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1." Therefore, the entire length of SEQ ID NO:1. Thus, claim 1 would be understood by one of skill in the art to encompass polypeptides having chemical and structural similarity to the polypeptide of SEQ ID NO:1 which are at least 90% identical to the polypeptide sequence of SEQ ID NO:1.

Hence, the meaning of the claims is clear. The Examiner has asserted that the claims are indefinite because it is not clear "which 90% identical sequences are or are not naturally occurring." As presented by Applicants, interpretation of a "naturally occurring amino acid sequence" is provided within the Specification, see for example pages 4-5 in which an amino acid sequence which is "natural"

is not "synthetic, semi-synthetic, or recombinant." Thus, withdrawal of this rejection is therefore requested.

Rejection of Claims 1 and 16 under 35 U.S.C. §102 (e)

Applicants travers the rejection of claims 1 and 16 for at least the following reasons. Kleyn *et al.* do not teach a polypeptide comprising SEQ ID NO:1 or polypeptides having 90% sequence identity to SEQ ID NO:1, therefore, claims 1 and 16 are not anticipated by Kleyn *et al.* Additionally, although not acquiescing to the stated reason for the rejections of claims 1 and 16, claim 1 c) has been deleted. The amendment removes recitation of "a biologically-active fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, said polypeptide retaining at least one function of a polypeptide comprising an amino acid sequence of SEQ ID NO:1." Therefore, claims 1 and 16 are not anticipated by Kleyn *et al.* and withdrawal of this rejection is requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Please charge Deposit Account No. **09-0108** in the amount of **$110.00** as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. 09-0108.

Respectfully submitted,

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